

Using organic acids to
resolve chief complaints
and improve quality of life in
chronically ill patients

Part VII

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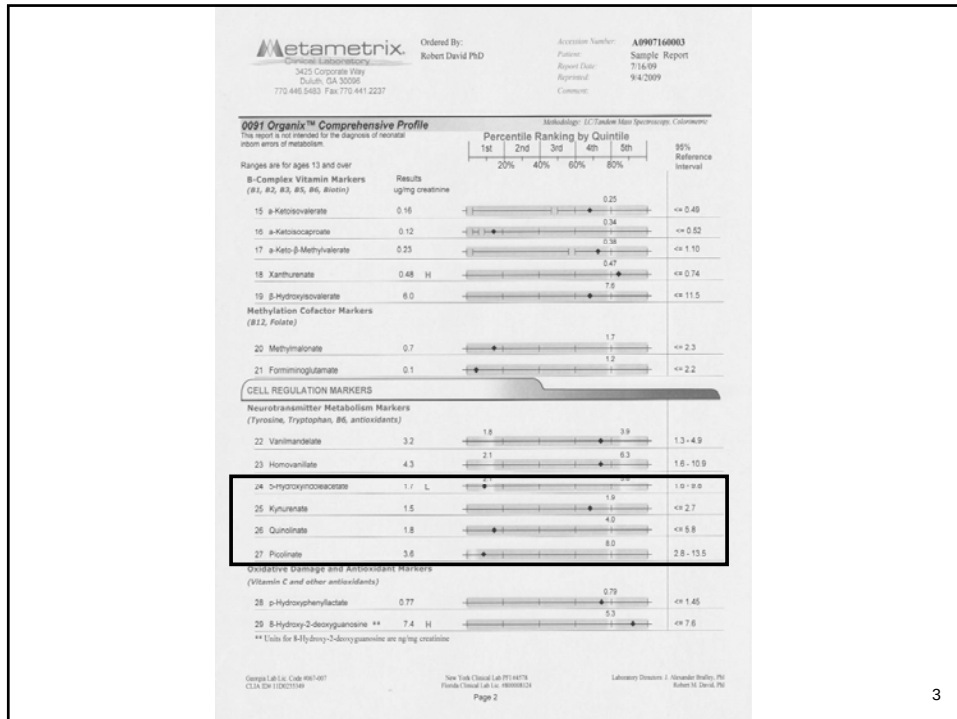
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Tryptophan metabolism
and
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Summer of Work Exposes Medical Students to System's Ills - NYTimes.com Page 1 of 3

The New York Times

September 9, 2009

Summer of Work Exposes Medical Students to System's Ills

By Jacob R. Gershowitz

SEATTLE — This summer, medical students from the University of Washington took a long look under the hood of the health care system they are about to inherit, and many returned to campus last week with their eyes wide open and their idealism tempered.

Summer of work exposes medical students to system's ills, *The New York Times*, September 9, 2009

The students learned not only to deliver babies and suture wounds, but also to order unnecessary tests as protection against lawsuits, to hector specialists into seeing Medicaid patients, to match patients with prescriptions on Wal-Mart's \$4 list. And they saw firsthand what Mr. Olgard called "a tidal wave of chronic disease" — diabetes, hypertension, obesity, depression — that left many questioning how much any one physician could really accomplish.

"I often wondered what we were actually doing to help people," Mr. Olgard said.

Not surprisingly, Mr. Olgard said, "You have to be realistic about the system. It's not going to be fixed overnight. It's a tidal wave of chronic illness..."

For its part, the University of Washington School of Medicine has dispatched its rising second-year students across the Northwest to provide primary care in rural or underserved areas. The monthlong program is elective, but a record number of students took part this year — 117 from a class of 216.

The school has a cooperative agreement to train medical students from Alaska, Idaho, Montana and Wyoming, none of which has a medical college of its own. The summer program is one of several vehicles, along with loan forgiveness endorsements, designed to lure students back to their home states to practice in areas with a shortage of primary care doctors.

This year, the students set out as negotiations were intensifying in Washington over wholesale changes to the health care system they will soon be joining. Whether there will be improvements to the system remains to be seen, but few students returned thinking there was little to fix.

http://www.nytimes.com/2009/09/09/health/policy/09medschool.html?_r=1&th=&mc=th&... 9/9/2009

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Organic Acids – Part VII

Dr. Jeff Moss



**Nestlé Nutrition Workshop Series
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Nutrition and Critical Care

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Baracos VE. Overview on metabolic adaptation to stress, pp. 1-13.

“An understanding of the nature of stress is fundamental to the rational design of nutrient mixtures to feed patients whose homeostasis has been altered by one or more stressors.”

“All stresses may be presumed to be associated with characteristic modifications in the metabolism of lipids, carbohydrates, amino acids, and micronutrients.”

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Clinical Nutrition (2004) 23, 1256-1266



REVIEW

Acute and “chronic” phase reaction—a mother of disease

Stig Bengmark

Department of Surgery and Liver Institute, UCL, London, UK

Received 23 July 2004

KEYWORDS

Acute phase response;
Chronic phase response;
Metabolic syndrome;
Cellular membranes;
Endothelial cells;
Abdominal obesity;
Insulin resistance;
Growth hormones;
Free fatty acids;
Alzheimer disease;
Parkinson disease;
Neurodegenerative diseases;
Atherosclerosis;
Coronary-vascular disease;
Cancer;
Breast cancer;
Colorectal cancer;
Prostatic cancer;
Diabetes;
Cirrhosis;
Fatty liver;
Gallbladder disease;
Chronic renal disease;

Summary The world is in diseases. Almost half of the mortality is due to these chronic diseases. And they are these diseases are associated consumption of calorie and also under-consumption of a function of the innate immune changes induced in response the subsequent development chronic diseases. The and importance, and the function of the underlying cells; their ability to obtain nutrients and antioxidants and to eliminate waste products. The abdominal adipocytes seem to play a key role, as they have the ability to in stressful situations release much of proinflammatory cytokines, PPAR- α and free fatty acids compared to elsewhere in the body. The load on the liver of these various substances in often of greater magnitude than the liver can handle. Some of the most common chronic diseases and their potential association with acute and “chronic” phase responses and metabolic syndrome are discussed separately. The need for studies with lifestyle modifications is especially emphasized.

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Bengmark S. Acute and “chronic” phase reaction – a mother of disease, *Clin Nutr*, Vol. 23, pp. 1256-66, 2004

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Organic Acids – Part VII

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Considerations for the Catabolic Patient				
Signs & Symptoms	Consider	Treatment Plan	Monitor	Supplementation
Signs & Symptoms: - Feeling "lousy" - Fatigue - Cravings - Depression/anxiety - Poor quality sleep - Poor digestion/absorption/leaky gut - Chronic pain/infection Clinical Findings: - High % body fat - Low bone density - High fasting insulin - Heavy metal burden - Calcium to phosphorus ratio 3:1 - High normal globulin - Cholesterol (220-280) - High LDL, low HDL - High triglycerides - Low normal serum potassium, high normal serum sodium - High normal BUN with normal creatinine - Low urinary sulfate - Genomic variations	Optimize pH	Optimize fluid and electrolyte balance	Morning urinary pH -pH paper	Potassium bicarbonate -K Alkaline (Moss) Magnesium -Magnesium Glycinate (Vital Nutrients)
	Optimize muscle mass (reduce sarcopenia) and amino acid levels	Pay special attention to protein and amino acids	Body composition: -Bioelectric impedance scale Grip strength: -dynamometer	Amino acids -Custom Amino Base (Metabolic Maint.) Protein powders/bars -UltraLean products (Biogenesis) -Paleo products (DFH)
	Reducing inflammation	Reduce inflammation Address food allergies	Inflammatory biomarkers: -HS-CRP -Fibrinogen levels -WBC -Differential	Anti-inflammatory agents -Inflametric (Olympian) -D-Flame (Protocols) -Pain Guard (Perque) Fish Oils -Ultra Pure Fish oil (Vital Nutrients) Food allergy blends -AllerGzymes (DFH)
	Improving insulin sensitivity	Watch carbohydrate/protein ratio	Fasting glucose Fasting insulin Cravings	Metabolic Synergy (DFH)
	Optimize dietary carbohydrate/protein ratios	Replete protein deficiencies and reduce carbohydrate intake along with improvements in dietary quality	Diet diary Optimal protein intake -1.0 – 1.2 g/kg body weight	Protein powders/bars -Paleo products (DFH) -UltraLean (Biogenesis)
	Optimize GI function	Dietary changes, supplementation of digestive aids	Patient signs and symptoms	Betaine HCl (Vital Nutrients) Digestzymes (DFH) Intestinal Repair Complex (Biogenesis)
	Optimize micronutrient deficiencies/imbbalances	Supplementation of multis Possible emphasis on vitamin D, iodine, and zinc	Serum 25 OH vitamin D Fatigue/serum thyroid indicators Zinc taste test	Multi Nutrients (Vital Nutr) Vitamin D (Vital Nutr) Iosol (Moss) Zinc Supreme (DFH)
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 Invited Review Neurosignals 2009;17:144-152 DOI: 10.1155/2009/144152		Received April 20, 2009 Accepted after revision June 5, 2009 Published online February 5, 2010
Biological Mechanism of Antidepressant Effect of Omega-3 Fatty Acids: How Does Fish Oil Act as a 'Mind-Body Interface'?		
Kuan-Pin Su Department of General Psychiatry and Mind-Body Interface Laboratory (MBI-LAB), China Medical University and Hospital, Taichung, Taiwan; Stress, Psychiatry and Immunology Laboratory (SPI-Lab), Institute of Psychiatry, King's College London, London, UK		
Key Words Major depressive disorder - Depressive acid - Docosahexaenoic acid - Arachidonic acid - Prostaglandins - Thromboxanes - Lipid Phospholipase A2 - Cyclo-oxygenase		
Abstract The unsatisfactory results of monoamine-based antidepressant therapy and the high occurrence of somatic symptoms and physical illness in patients with depression imply that the serotonin hypothesis is insufficient to approach the aetiology of depression. Depressive disorders with somatic presentation are the most common form of depression. Somatization, the bodily symptoms without organic explanation, is similar to cytokine-induced sickness behaviour. Based on recent evidence, omega-3 polyunsaturated fatty acids (n-3 PUFAs, or n-3 fatty acids) are enlightening a promising path to discover the unsolved of depression, sickness behaviour and to link the connection of mind and body. The PUFAs are classified into n-3 (or omega-3) and n-6 (or omega-6) groups. Eicosapentaenoic acid and docosahexaenoic acid, the major bioactive components of n-3 PUFAs, are not efficiently synthesized in humans and should therefore be obtained directly from the diet, particularly by consuming fish. Docosahexaenoic acid deficiency is associated with dysfunctions of neuronal membrane stability and transmission		
prostaglandin E ₂ synthesis, which might be linked to the somatic manifestations and physical comorbidity in depression. The role of n-3 PUFAs in immunity and mood function supports the promising hypothesis of psychoneuroimmunology of depression and provides an excellent interface between 'mind' and 'body'. This review is to provide an overview of the evidence about the role of n-3 PUFAs in depression and its common comorbid physical conditions and to propose mechanisms by which they may modulate molecular and cellular functions.		
Introduction Major depressive disorder (MDD) is a serious psychiatric illness with a high lifetime prevalence rate [1]. However, the current treatment for this high burden disease is not satisfactory. Less than 50% of patients achieve full remission with optimized medication treatment [2] despite that more than 40 antidepressants with mechanisms related to serotonin, norepinephrine and/or dopamine		
KARGER © 2009 S. Karger AG, Basel 1661-8747/09/1702-144\$28.00 DOI: 10.1155/2009/144152 www.karger.com	Dr. Kuan-Pin Su Department of Psychiatry China Medical University Hospital No. 2, Yuh-Der Road, Taichung 40452 (Taiwan) Tel.: +886 4 2205 2121, ext. 3070; Fax: +886 4 2206 1230; E-Mail: kalsu@cmuh.org.tw	Copyright © 2009 S. Karger AG, Basel

Table 1. Overlapping of symptoms of acute sickness behaviour associated with IFN- α therapy and the somatic symptoms in MDD

Symptoms	Prevalence in IFN- α therapy ^a , %	Prevalence in MDD ^b , %
Fatigue/asthenia	39–90	73
Headache	27–67	33 ^e
Gastrointestinal symptoms	50 ^{c, 1}	34–47 ^f
Psychomotor slowing	40 ^c	59–65 ^f
Insomnia	20–39 ^d	63
Irritability	35 ^d	50
Arthralgia	9–36	31 ^e
Musculoskeletal pain	26–32	62–80 ^{g, 2}
Abdominal pain	15–20	21 ^e
Anorexia	13–19	40
Anxiety	13–18 ^d	57
Poor concentration	14 ^d	51

^a [46], unless otherwise specified; ^b [99], unless otherwise specified; ^c [100]; ^d [101]; ^e [102]; ^f [103]; ^g [104].

¹ Nausea, vomiting, bowel problems.

² Result from depressed inpatient population.

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Modulation of tryptophan and serotonin: The big picture

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The big picture

- Traditional allopathic approaches have primarily revolved around neurotransmitter modulation – particularly serotonin
- ***How well has it worked?***

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REVIEW

Antidepressant Drug Effects and Depression Severity
A Patient-Level Meta-analysis

Jay C. Fournier, MA
Robert J. Deldolus, PhD
Steven D. Hollon, PhD
Soma Dismidjian, PhD
Jay D. Amsterdam, MD
Richard G. Shelton, MD
Jon Tweney, MD

Context Antidepressant medications represent the best established treatment for major depressive disorder, but there is little evidence that they have a specific pharmacological effect relative to pill placebo for patients with less severe depression.

Objective To estimate the relative benefit of medication vs placebo across a wide range of initial symptom severity in patients diagnosed with depression.

Data Extraction Individual patient-level data were obtained from study authors.

Results In patients with mild to moderate depression, the magnitude of benefit of antidepressant medication compared with placebo was minimal or non-existent, on average. In patients with very severe depression, the benefit of medications over placebo was substantial.

Conclusion The magnitude of benefit of antidepressant medication compared with placebo increases with severity of depression symptoms and may be minimal or non-existent, on average with mild or moderate symptoms. For patients with very severe depression, the benefit of medications over placebo is substantial.

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The big picture

- For years we have taken a similar approach:
- Using nutraceuticals/herbals to modulate neurotransmitter activity

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The big picture: What approaches do we use?

- Symptom/disease-based protocols
- Protocols based on neurotransmitter and/or neurotransmitter metabolite measurement

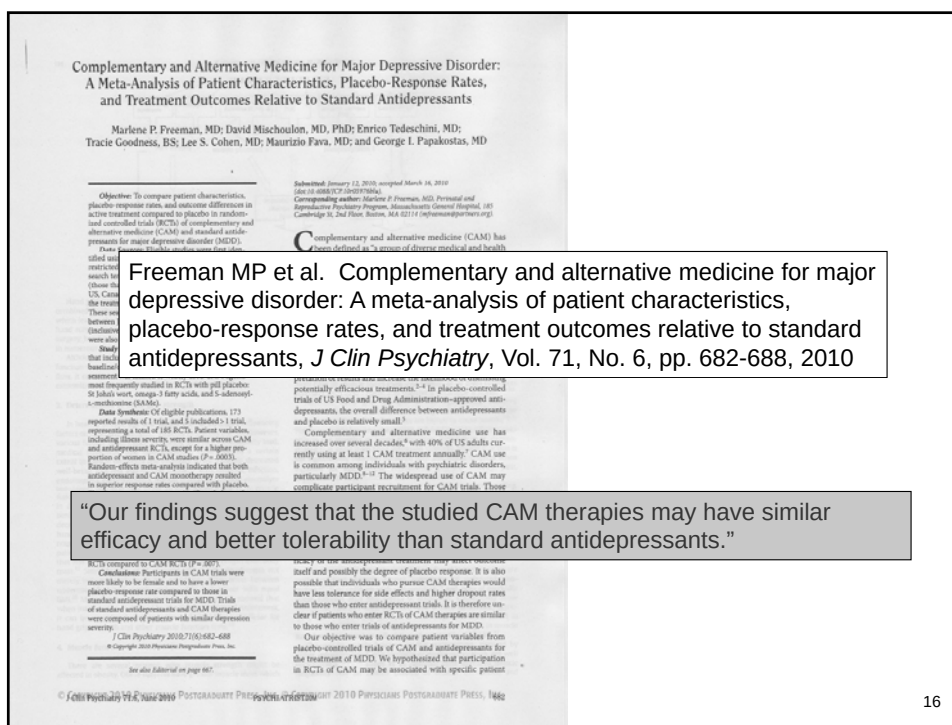
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The big picture:

How well have these approaches worked?

- Clinical feedback has been highly variable.
- Results from controlled trials has been highly variable.

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- “Overall, we found that both CAM therapies and antidepressants were superior to placebo.”
- “It is important to assess depression severity at baseline when comparing studies, as depression severity at baseline is an independent predictor of the differential response between active antidepressant and placebo response.”
- “There has been controversy due to inconsistent results with St. John’s wort across large studies as whether it is effective for moderate to severe depression.”

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- “Because CAM therapies are widely used and have good apparent acceptability among the general population, we expected that placebo-response rates might be higher in CAM than antidepressant studies.”
- “Interestingly, there was a lower placebo-response rate for patients enrolled in CAM studies compared with antidepressant studies.”
- “One possible explanation for the lower placebo-response rate in CAM trials is that participants in CAM studies may have more modest expectations compared to those randomized into trials of antidepressants.”

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The big picture:
Why aren't we replicating what we hear
about in major symposiums

- Placebo effect
- Expert practitioner/lecturers are not reporting all modalities employed
- Selected case reports do not give an accurate representation of overall outcome.

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The big picture:
Downside of success with current approaches
that focus on neurotransmitter modulation

- ***They do not deal with the cause!!***
- ***Therefore, this is not functional medicine in its truest sense!!***

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The big picture: The downside of success

- Long term use
- Cost
- Risk of habituation

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Review
Adjuvant use of nutritional and herbal medicines with antidepressants, mood stabilizers and benzodiazepines
Jerome Sarris^{a,*}, David J. Kavanagh^b, Gerard Byrne^a

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ABSTRACT
Adjuvant use of nutritional and herbal medicines has potential to increase the efficacy of synthetic pharmacologicals, and perhaps also decrease their side-effects by allowing lower doses to be prescribed. We evaluated current evidence for adjuvant use of nutritional and herbal medicines with antidepressants, mood stabilizers and benzodiazepines.

Keywords:
Adjuvant
Antidepressants
Herbal medicine
Mood stabilizers
Benzodiazepines
Nutrition
In John's wort

Sarris J et al. Adjuvant use of nutritional and herbal medicines with antidepressants, mood stabilizers and benzodiazepines, *J Psychiatric Res*, Vol. 44, pp. 32-41, 2010

“Common sense suggests that a ‘one-size fits all’ approach often adopted in clinical trials may have less success than tailored prescriptions treating the cause/s of the individual's depression...”

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E-mail address: j.sarris@uq.edu.au (J. Sarris).

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- “In the case of nutritional adjuvancy, a beneficial effect may more likely occur when specific deficiencies or neurological dysregulations are apparent.”
- “For example, a patient who does not eat any omega-3 containing foods may potentially benefit more from adjuvant omega-3 prescription than a patient who regularly eats deep sea fish.”

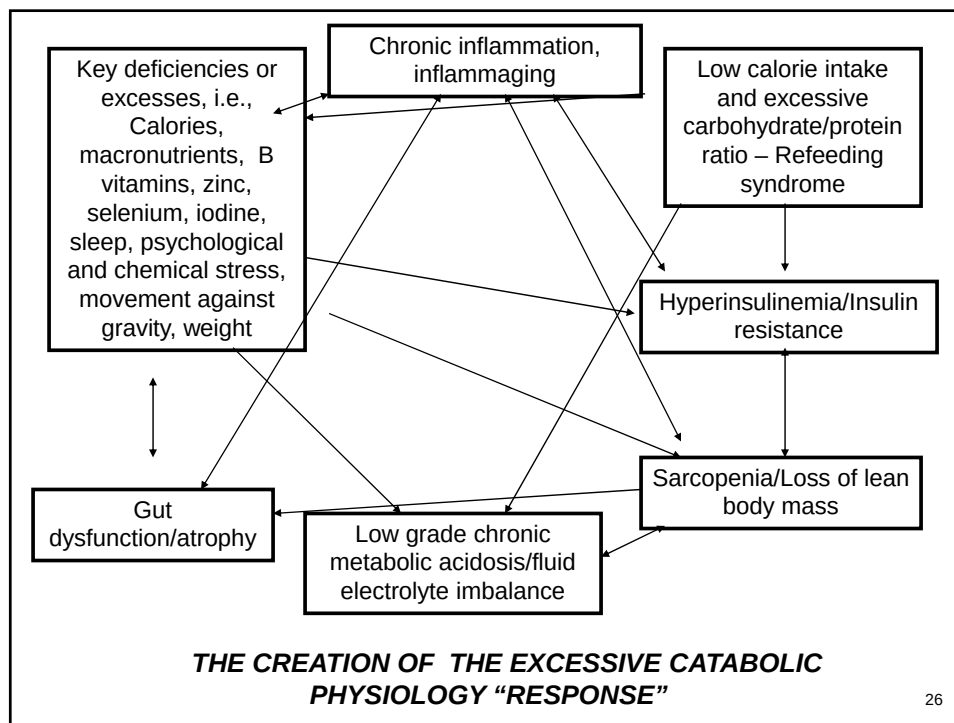
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- “Common deficiencies affecting mental health outcomes may involve amino acids (e.g. tryptophan, phenylalanine, tyrosine), which provide precursors to neurochemicals; B vitamins in particular B⁶, B¹², folate, which are involved in methylating pathways; and omega-3, which encourages neuronal communication.”

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Chronic inflammation!!

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Organic Acids – Part VII

Dr. Jeff Moss

Considerations for the Catabolic Patient				
Signs & Symptoms	Consider	Treatment Plan	Monitor	Supplementation
Signs & Symptoms: - Feeling "lousy" - Fatigue - Cravings - Depression/anxiety - Poor quality sleep - Poor digestion/absorption/leaky gut - Chronic pain/infection Clinical Findings: - High % body fat - Low bone density - High fasting insulin - Heavy metal burden - Calcium to phosphorus ratio 3:1 - High normal globulin - Cholesterol (220-280) - High LDL, low HDL - High triglycerides - Low normal serum potassium, high normal serum sodium - High normal BUN with normal creatinine - Low urinary sulfate - Genomic variations	Optimize pH	Optimize fluid and electrolyte balance	Morning urinary pH -pH paper	Potassium bicarbonate -K Alkaline (Moss) Magnesium -Magnesium Glycinate (Vital Nutrients)
	Optimize muscle mass (reduce sarcopenia) and amino acid levels	Pay special attention to protein and amino acids	Body composition: -Bioelectric impedance scale Grip strength: -dynamometer	Amino acids -Custom Amino Base (Metabolic Maint.) Protein powders/bars -UltraLean products (Biogenesis) -Paleo products (DFH)
	Reducing inflammation	Reduce inflammation Address food allergies	Inflammatory biomarkers: -HS-CRP -Fibrinogen levels -WBC -Differential	Anti-inflammatory agents -Inflametric (Olympian) -D-Flame (Protocols) -Pain Guard (Perque) Fish Oils -Ultra Pure Fish oil (Vital Nutrients) Food allergy blends -AllerGzymes (DFH)
	Improving insulin sensitivity	Watch carbohydrate/protein ratio	Fasting glucose Fasting insulin Cravings	Metabolic Synergy (DFH)
	Optimize dietary carbohydrate/protein ratios	Replete protein deficiencies and reduce carbohydrate intake along with improvements in dietary quality	Diet diary Optimal protein intake -1.0 – 1.2 g/kg body weight	Protein powders/bars -Paleo products (DFH) -UltraLean (Biogenesis)
	Optimize GI function	Dietary changes, supplementation of digestive aids	Patient signs and symptoms	Betaine HCl (Vital Nutrients) Digestzymes (DFH) Intestinal Repair Complex (Biogenesis)
	Optimize micronutrient deficiencies/imbbalances	Supplementation of multis Possible emphasis on vitamin D, iodine, and zinc	Serum 25 OH vitamin D Fatigue/serum thyroid indicators Zinc taste test	Multi Nutrients (Vital Nutr) Vitamin D (Vital Nutr) Iosol (Moss) Zinc Supreme (DFH)
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Available online at www.sciencedirect.com SCIENCE @ DIRECT® Clinica Chimica Acta 364 (2006) 82–90 Review Monitoring tryptophan metabolism in chronic immune activation Katharina Schröcksnadel, Barbara Wirltner, Christiana Winkler, Dietmar Fuchs * Division of Biological Chemistry, Biocentre, Innsbruck Medical University, Fritz Pregl Strasse 2, A-6020 Innsbruck, Austria Ludwig Boltzmann Institute of AIDS Research, Innsbruck, Austria Received 22 April 2005; received in revised form 10 June 2005; accepted 14 June 2005 Available online 1 September 2005	
Abstract The essential amino acid tryptophan is a constituent of proteins and is also a substrate for two important biosynthetic pathways: the generation of serotonin (5-hydroxytryptamine) by tryptophan 5-hydroxylase and the formation of indoles by indoleamine 2,3-dioxygenase (IDO) and indoleamine 2,3-dioxygenase-like (TDO) and indoleamine 2,3-dioxygenase-like (TDO) in part of the tryptophan catabolism. In chronic immune activation, low tryptophan concentrations may contribute to immunodeficiency. Decreased serum tryptophan can also affect serotonin biosynthesis and thus contribute to impaired quality of life and depressive mood. As such, monitoring tryptophan metabolism in chronic immunopathology provides a better understanding of the association between immune activation and IDO and its role in the development of immunodeficiency, anemia and mood disorders. © 2005 Elsevier B.V. All rights reserved. Keywords: Tryptophan; Indoleamine (2,3)-dioxygenase; Depression	Contents 1. Tryptophan metabolism 83 2. IDO in lipid cellular growth via tryptophan degradation 83 3. Measurement of tryptophan and kynurenine 84 4. Accelerated tryptophan catabolism due to IDO activation in patients 85 4.1. Infection 85 4.2. Malignancy 85 4.3. Other diseases 85 4.4. Pregnancy 86 4.5. Immunomodulatory treatment 86 5. Pathogenetic effects related to accelerated tryptophan degradation 86 5.1. Immunodeficiency, anemia, cachexia 86 5.2. Mood changes 87
* Corresponding author. Tel.: +43 512 507 2519; fax: +43 512 507 2865. E-mail address: Dietmar.Fuchs@iuh.at (D. Fuchs). 0009-8951/\$ - see front matter © 2005 Elsevier B.V. All rights reserved. doi:10.1016/j.cca.2005.06.013	

- “The essential amino acid L-tryptophan is required for the biosynthesis of proteins and is precursor for several biologically important compounds: (a) 5-hydroxytryptamine (serotonin) which is formed by tryptophan (5)-hydroxylase following decarboxylation; (b) tryptophan (2,3)-dioxygenase (TDO, tryptophan pyrrolase); and (c) indoleamine (2,3)-dioxygenase (IDO).”

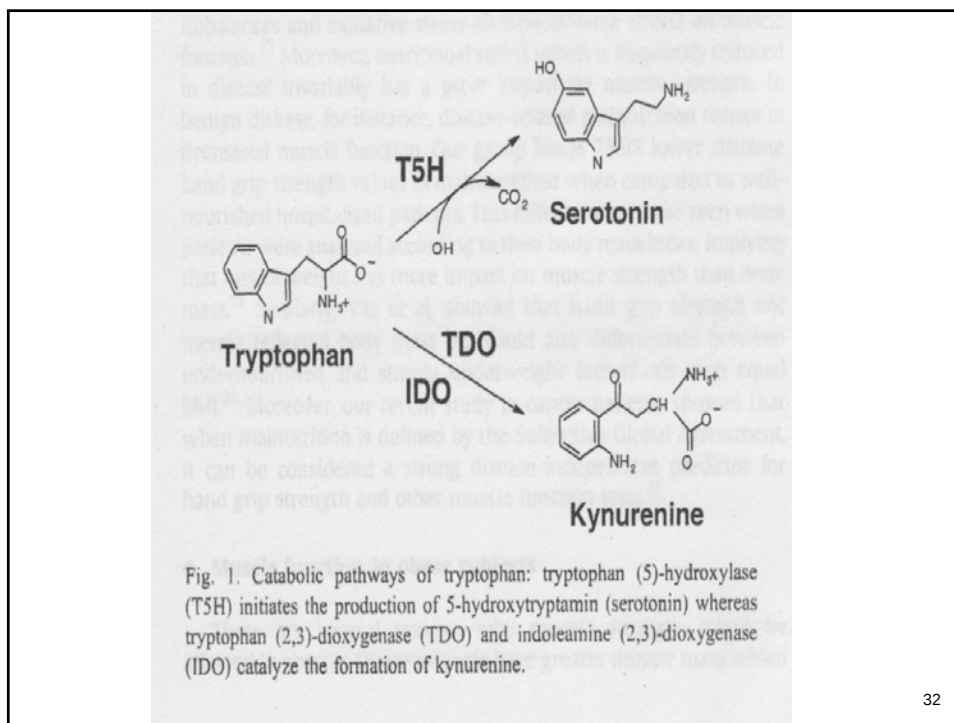
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- “The latter two catabolize tryptophan via the so-called kynurenine-pathway synthesizing nicotinic acid, the vitamin niacin and nicotinamide adenine dinucleotides as end products.”
- “Although TDO is localized to the liver and is up-regulated by corticosteroids, IDO is expressed by a variety of cells and is inducible preferentially by Th1-type cytokine interferon- γ (IFN- γ).”

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- “Similar to TDO, IDO catalyzes the first step in tryptophan degradation, i.e., formation of N-formylkynurenine which subsequently deformylates to kynurenine.”

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- “In vivo, enhanced cytokine-induced degradation of tryptophan is observed whenever the cellular (Th1-type) immune response is induced.”
- “In this case, a decrease in serum tryptophan concentration and concomitant increase in kynurenine or other tryptophan catabolites can be detected.”

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- “Under normal conditions, kynurenine concentration is related to tryptophan level.”
- “Reduced dietary intake of tryptophan lowers endogenous tryptophan level. Under these circumstances, lower kynurenine concentration is also observed.”

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- “The kynurenin (kyn) to tryptophan (trp) ratio (kyn/trp), i.e., the ratio of the concentration of the first product of TDO and IDO versus their substrate is an appropriate indicator of tryptophan degradation.”
- “The kyn/trp ratio provides a better and normalized measurement than absolute tryptophan or kynurenine concentration.”

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- “To substantiate that tryptophan degradation is due to activation of IDO rather than TDO it is necessary to demonstrate concomitant immune system activation.”
- “Thus, activated IDO is indicated when kyn/trp correlates with an immune activation parameter and endogenous IFN- γ formation.”

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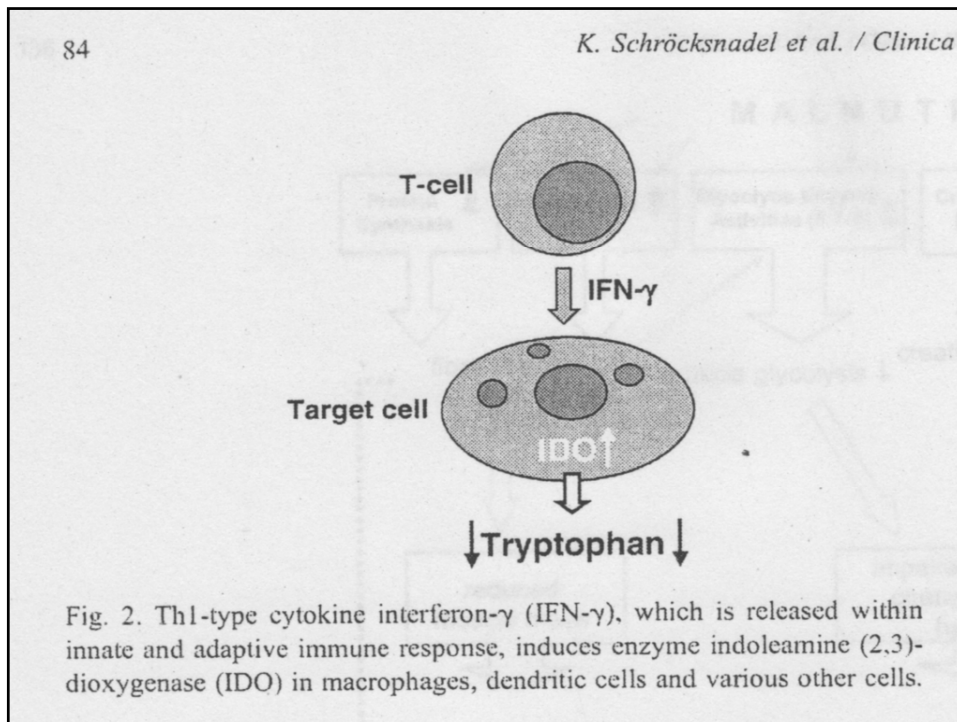


Table 1

Relationship between tryptophan metabolic changes and immune activation

	Changes of blood levels			Immune activation markers
	Tryptophan	Kynurenine	Kyn/trp	
Insufficient dietary intake	↓	↓	↔	↔
TDO	↓	↑	↑	↔
IDO	↓↓	↑↑	↑↑	↑↑

- “IDO activation limits availability of tryptophan.”
- “Because tryptophan is required for protein synthesis, withdrawal of this essential amino acid from the micro-environment arrests protein biosynthesis and subsequent growth of pathogens and proliferating cells.”

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- ***“Consequently, tryptophan depletion is regarded as a defense mechanism induced by IFN- γ in immunocompetent cells during immune response.”***
- ***“This phenomenon acts as an antimicrobial or antitumoral effector mechanism and limits the growth of intracellular pathogens or malignant cells.”***

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- "...in addition to tryptophan deprivation, the apoptotic effect of certain tryptophan catabolites such as kynurenine is also important."
- ***"These observations support the view that activation of IDO together with other biochemical pathways induced by IFN- γ represents an important antiproliferative mechanism of monocyte-derived macrophages and dendritic cells."***
- "This phenomenon, however, can also decrease the response of stimulated T-cells and thus contribute to development of immunodeficiency."

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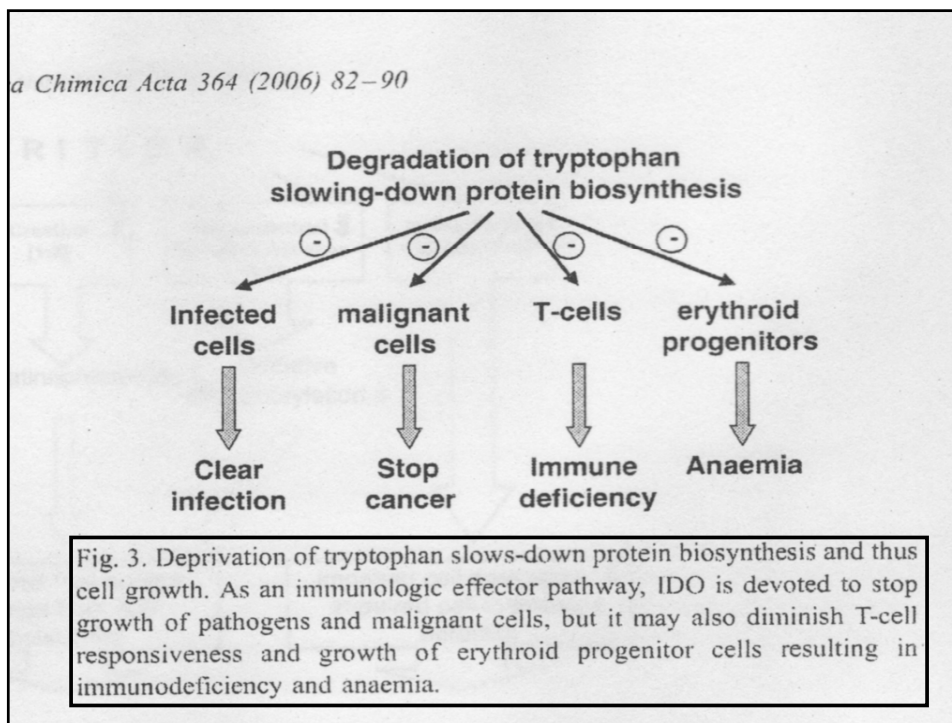


Table 2

List of clinical conditions characterized by tryptophan degradation associated with increased immune activation (References in brackets)

Infection

HIV infection [9,28–30], neuroborreliosis [35], sepsis [33], *Streptococcus pyogenes* infection [34]

Autoimmune syndromes

Rheumatoid arthritis [44,45], systemic lupus erythematosus [43], inflammatory bowel disease [36]

Malignancy

Adult T-cell leukaemia [41], colon carcinoma [36,37], colorectal cancer [42], gynaecological cancer [38], haematological neoplasias [12]

Neurodegenerative disorders

Alzheimer's disease [46], Huntington's disease [47], Parkinson's disease [48]

Other conditions

Cardiovascular disease [11], major depression [66], cytokine treatment [6,53,54], pregnancy [50–52]

“It is important to note that increased tryptophan degradation and signs of immune activation are common during normal aging.”

- “Accelerated catabolism of tryptophan appears to play a role in the pathogenesis of the anemia of inflammation as well as in weight loss and the development of cachexia.”
- “Recently an association between lowered tryptophan concentration and drop in hemoglobin was reported in patients with anemia of inflammation.”

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Mood changes
and
tryptophan availability

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- “Decreased tryptophan availability reduces the biosynthesis of neurotransmitter 5-hydroxytryptamine (serotonin) which can increase susceptibility for development of mood disturbances and depression and also impair cognitive function.”
- “Immune-mediated tryptophan degradation by IDO may thus elicit neuropsychiatric symptoms when the availability of tryptophan is insufficient for normal serotonin biosynthesis.”

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- “The concentration of kynurenine and other catabolites such as quinolinic acid accumulate as a consequence of tryptophan degradation.”
- “The latter is a potent neurotoxin which interferes with the NMDA receptor and may therefore additionally influence the neuroendocrine system.”

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- “Major depression is closely related to disturbed tryptophan metabolism.”
- “Reduced concentration of 5-hydroxyindolacetic acid, the main catabolite of serotonin, confirms insufficient availability of serotonin.”

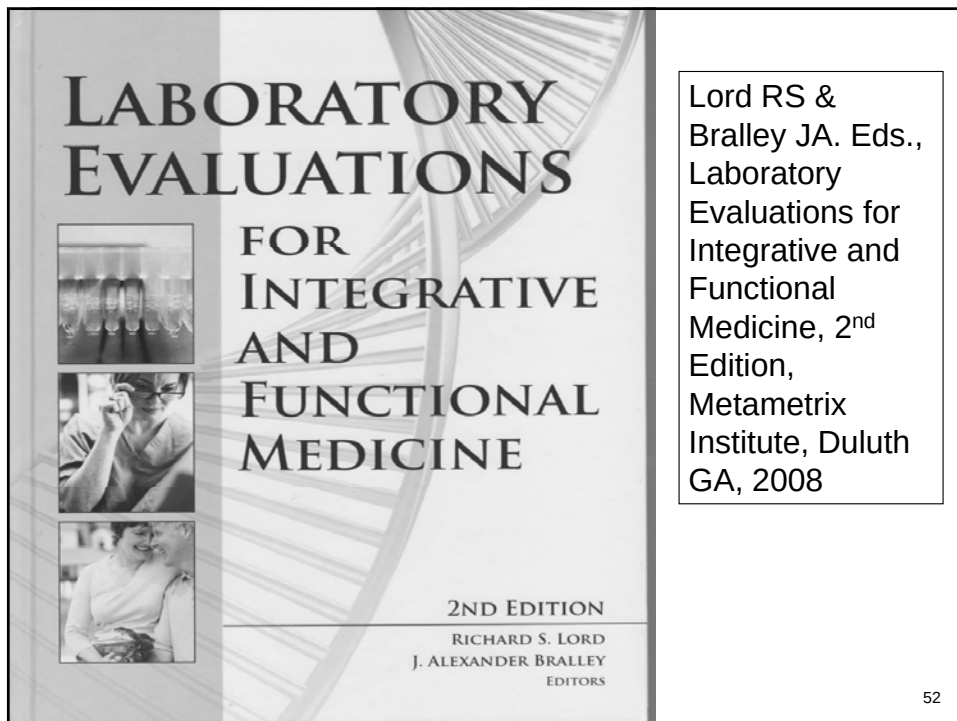
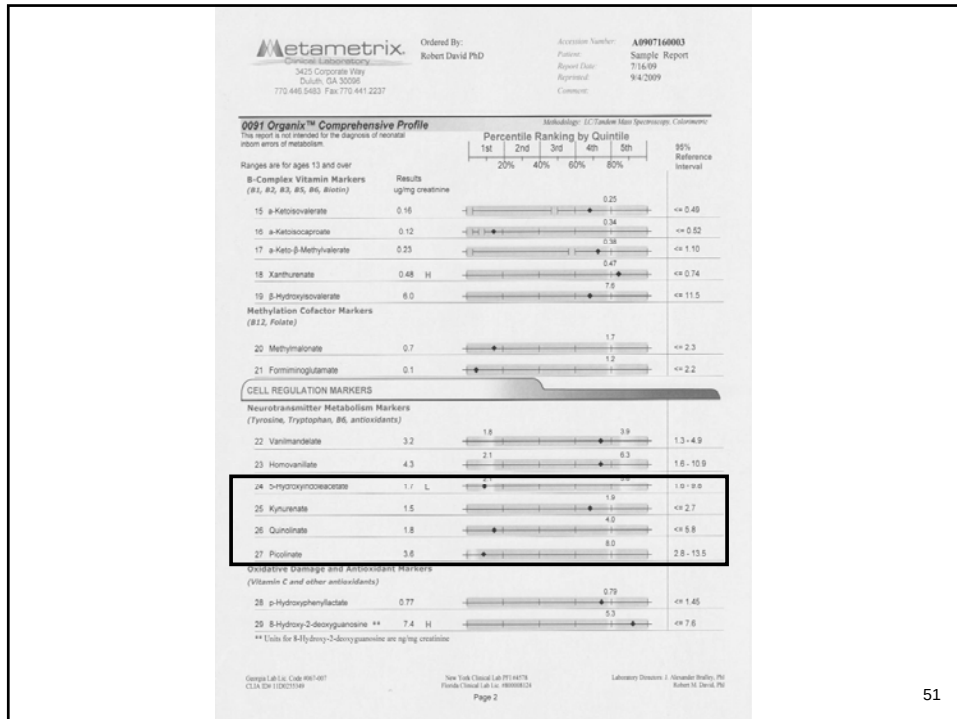
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“...enhanced degradation of tryptophan due to immune stimulation could underlie the increased risk for development of depression in patients with chronic inflammatory diseases in general and specifically during normal aging.”

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Dr. Jeff Moss



Thank you!!

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